CLASSIFICATION, PREVENTION AND TREATMENT

CLASSIFICATION SYSTEMS

- *The Meggitt–Wagner classification* is the most well-known and validated system for foot ulcers, and is shown in Table 2.1. The advantages and disadvantages of this classification system are described in Table 2.2.
- '*The University of Texas classification system for diabetic foot wounds*', (Table 2.3) has recently been proposed and validated by the University of Texas. This system evaluates both depth of the ulcer — as in Meggitt–Wagner classification system — and presence of infection and ischemia. Uncomplicated ulcers are classified as stage A, infected ulcers as stage B, ulcers with ischemia as

Table 2.1 Meggitt–Wagner classification of foot ulcers

Grade	Description of the ulcer
Grade 0	Pre- or post-ulcerative lesion completely epithelialized
Grade 1	Superficial, full thickness ulcer limited to the dermis, not extending to the subcutis
Grade 2	Ulcer of the skin extending through the subcutis with exposed tendon or bone and without osteomyelitis or abscess formation
Grade 3	Deep ulcers with osteomyelitis or abscess formation
Grade 4	Localized gangrene of the toes or the forefoot
Grade 5	Foot with extensive gangrene

Table 2.2 Advantages and disadvantages of the Meggitt–Wagner classification system

Advantages

- It is simple to use and has been validated in a number of studies
- Higher grades are directly related to increased risk for lower limb amputation
- It provides a guide for planning treatment
- It is considered the gold-standard, against which other systems should be validated

Disadvantages

- Although the presence of infection and ischemia are related to poor outcome, ischemia in patients classified into grades 1–3 and infection in grade 1, 2 and 4 patients is not taken into account
- The location of the ulcer is not described
- Patient-related factors (poor foot care, emotional upset, denial) and foot deformities are not evaluated

Table 2.3 'The University of Texas classification system for diabetic foot wounds'

Stage	Grade 0	Grade 1	Grade 2	Grade 3
A	Pre- or post-ulcerative lesion completely epithelialized	Superficial wound not involving tendon, capsule or bone	Wound penetrating to tendon or capsule	Wound penetrating to bone or joint
B	With infection	With infection	With infection	With infection
C	With ischemia	With ischemia	With ischemia	With ischemia
D	With infection and ischemia	With infection and ischemia	With infection and ischemia	With infection and ischemia

Table 2.4 Advantages and disadvantages of 'The University of Texas classification system'

Advantages
• It is simple to use and more descriptive
• It has been evaluated and shown to predict more accurately the outcome of an ulcer (healing or amputation) than the Meggitt–Wagner classification.
• Cases with infection and/or ischemia are taken into account in this system
• It provides a guide for planning treatment
Disadvantages
• Patient-related factors (poor foot care, emotional upset, denial) and foot deformities are not evaluated
• The location of the ulcer is not described

stage C and ulcers with both infection and ischemia as stage D. Grades 1 and 2 are similar to the Meggitt–Wagner classification. Grade 3 ulcers are ulcers penetrating the bone or joint. The higher the grade, and the stage of an ulcer, the greater the risk for non-healing or amputation. The advantages and disadvantages of 'The University of Texas classification system' are described in Table 2.4.

In addition to these two classification systems, other systems have been proposed:

- Edmonds and Foster have proposed a simpler classification. According to this system, based on clinical tests and determination of the ankle brachial pressure index, foot ulcers are classified into neuropathic and neuro-ischemic.
- Brodsky suggested the *'depth-ischemia' classification*, which is a modification of the Meggitt–Wagner classification. According to this proposal, ulcers are classified into four subgroups (A, not ischemic; B, ischemic without gangrene; C, partial gangrene of the foot; and D, complete foot gangrene) with grades 0–3 (similar to the Meggitt–Wagner classification).
- Macfarlane and Jeffcoate proposed the *S(AD)SAD classification* for diabetic foot ulcers. According to this system, ulcers are classified on the basis of size (area and depth), presence of sepsis, arteriopathy, and denervation. This system awaits clinical validation.

Any valid classification system of foot ulcers should facilitate appropriate treatment, simplify monitoring of healing progress and serve as a communication code across specialties in standardized terms. Despite its disadvantages, the 'University of Texas classification system' offers many advantages over the Meggitt–Wagner system and is the most appropriate system devised to date. In addition, inclusion in a classification system of other parameters such as location of the ulcer, foot deformities and other factors which may be related to the outcome of an ulcer, makes the system more complex and cumbersome. 'The University of Texas classification system' is expected to be widely adopted in the future.

CLINICAL PRESENTATION OF NEUROPATHIC, ISCHEMIC AND NEURO-ISCHEMIC ULCERS

- Neuropathy is present in about 85–90% of foot ulcers in patients with diabetes.
- Ischemia is a major factor in 38–52% of cases of foot ulcers.

NEUROPATHIC ULCERS (FIGURES 2.1–2.3)

- Develop at areas of high plantar pressures (metatarsal heads, plantar aspect of

Figure 2.1 Typical neuropathic ulcer with callus formation on the first metatarsal head before debridement

Figure 2.2 Neuropathic ulcer on the first metatarsal head with healthy granulating tissue on its bed

Figure 2.3 Neuropathic ulcer on the first metatarsal head with healthy granulating tissue on its bed and callus formation

the great toe, heel or over bony prominences in a Charcot-type foot).

- Are painless, unless they are complicated by infection.
- There is callus formation at the borders of the ulcer.
- Its base is red, with a healthy granular appearance.
- On examination evidence of peripheral neuropathy (hypoesthesia or complete loss of sensation of light touch, pain, temperature, and vibration, absence of Achilles tendon reflexes, abnormal vibration perception threshold, often above 25 V, loss of sensation in response to 5.07 monofilaments, atrophy of the small muscles of the feet, dry skin and distended dorsal foot veins) is present. However, the pattern of sensory loss may vary considerably from patient to patient.

Figure 2.4 Ischemic ulcer under the heel in a patient with severe peripheral vascular disease

- The foot has normal temperature or may be warm.
- Peripheral pulses are present and the ankle brachial pressure index is normal or above 1.3.

ISCHEMIC ULCERS (FIGURES 2.4–2.8)

- Develop on the borders or the dorsal aspect of the feet and toes or between toes.
- They are usually painful.

Figure 2.5 Ischemic ulcer on the dorsum of the second toe in a patient with critical limb ischemia. Case discussed in Chapter 7

Figure 2.6 Dry gangrene of the fifth right toe. Redness, and edema, which are typical signs of infection involving the forefoot, are present

- There is usually redness at the borders of the ulcer.
- Its base is yellowish or necrotic (black).
- There is a history of intermittent claudication.
- On examination indications of peripheral vascular disease (skin is cool, pale or cyanosed, shiny and thin, with loss of hair, and onychodystrophy; peripheral pulses are absent or weak; the ankle brachial index is <0.9) are present.
- Non-invasive vascular testing (duplex or triplex ultrasound examination,

Figure 2.7 Ischemic ulcer after sharp debridement of the gangrene shown in Figure 2.6

Figure 2.8 Ischemic ulcer on the tip of the third right toe, with necrotic center

segmental pressures measurement, plethysmography), and angiography confirm peripheral vascular disease.

- There are no findings of peripheral neuropathy.

MIXED ETIOLOGY ULCERS (NEURO-ISCHEMIC ULCERS) (FIGURES 2.9 AND 2.10)

Neuro-ischemic ulcers have a mixed etiology, i.e. neuropathy and ischemia, and a mixed appearance.

PREVENTION OF FOOT ULCERS

Based on the results of clinical examination, and/or laboratory testing and imaging studies, every patient with diabetes may be classified on the basis of the risk for foot problems (Table 2.5). This classification helps as a guide for patient management. Patients with active foot ulcers are not included in this classification.

Inappropriate footwear is a major cause of ulceration. The aim of providing special shoes and insoles (preventive foot wear) to diabetic patients at risk for foot ulceration, is to reduce peak plantar pressure over areas 'at risk', and to protect their feet against injuries from friction. Although there is limited scientific information about shoe selection, recommendations can be made in this regard, based on risk

Figure 2.9 Neuro-ischemic ulcer on heel. This was a painless ulcer due to severe diabetic peripheral neuropathy. Another neuro-ischemic ulcer is seen under the first metatarsal head. Claw toes and lateral plantar cracks on the midfoot are also evident

Table 2.5 Classification of categories of diabetic patients based on the risk for ulceration

Risk category	
0	Protective sensation is intact; the patient may have foot deformity
1	Loss of protective sensation
2	Loss of protective sensation and high plantar pressure, or callosities, or history of foot ulcer
3	Loss of protective sensation and history of ulcer, and severe foot or toe deformity and/or limited joint mobility; significant peripheral vascular disease

(Modified from Chantelau E. Footwear for the high-risk patient. In Boulton AJM, Connor H, Cavanagh PR (Eds), *The Foot in Diabetes* (3rd edn). Chichester: Wiley, 2000; 131–142, with permission).

stratification studies. Shoes for the patient at risk for ulceration should have certain characteristics. High heel shoes are completely inappropriate, as they shift body weight towards the forefoot, and increase pressure under the metatarsal heads. Patients with toe deformities need shoes with sufficient room in the toe box to prevent

Figure 2.10 Neuro-ischemic ulcer in the medial aspect of the right first metatarsal head with fibrous tissue and necrosis on its bed

friction and pressure on the dorsum of the toes.

A recent study from the UK estimated that providing preventive footwear for 700 patients at risk for foot ulceration per year (with an average total cost of €179,000), would only need to prevent two below-knee amputations per year in order to be cost-effective, since the total cost of an amputation procedure is about €88,000.

Foot deformity is defined according to the 'International Consensus on the Diabetic Foot' as 'the presence of structural abnormalities of the foot such as presence of hammer toes, claw toes, hallux valgus, prominent metatarsal heads, status after neuro-osteoarthropathy, amputations or other foot surgery'. Additional foot deformities which can also lead to foot ulceration are described in other chapters of this book.

RISK CATEGORY 0

Patients in this category are characterized by preserved protective sensation and normal blood supply to their feet. These patients should have their feet examined on an annual basis, as asymptomatic nerve or vascular damage may develop. There is no need for special footwear. Patients should be instructed to choose shoes of proper style and fit, which pose no risk to their feet should they develop loss of sensation or inadequate blood supply to the feet. Athletic footwear is a good choice.

RISK CATEGORY 1

Correct foot care should be explained to all patients classified in categories 1–3, and these patients should be examined in the outpatient diabetes clinic every 4 months. Loss of protective sensation should be 'replaced' by increased awareness of situations which threaten the foot. Patients in category 1 are at twice the risk of developing foot ulcers than those in category 0. Particular care should be taken when these patients buy new shoes. Patients with loss of protective sensation tend to select shoes which are too small because they are more able to feel a tight shoe. Shoes should not be too loose either. The inside of the shoe should be 1–2 cm longer than the foot itself. The internal width should be equal to the width of the foot at the metatarsophalangeal joints. The fitting must be carried out with the patient in the standing position and preferably at the end of the day.

All patients with loss of protective sensation should have soft, shock-absorbing stock insoles in all shoes they wear. Such insoles are usually made of open cell urethane foam, microcellular rubber or polyethylene foam (plastazote). According to the design of the insole and the material used, peak plantar pressure reduction during walking may range from 5 to 40%. As insoles may take up considerable space inside the shoe, care should be taken to allow sufficient room for the dorsum of the foot (by the use of extra depth stock shoes) otherwise ulceration may develop in this area. Many materials used in footwear lose their effectiveness in a relatively short time, depending on the patient's degree of activity. Therefore, regular replacement of the insoles is necessary at least three times a year. Shoes should also be changed at least once a year. Some specifically designed socks (padded socks) may be also be used, since these reduce peak plantar pressures during walking by up to 30%.

EDUCATING PATIENTS IN APPROPRIATE FOOT CARE

Education of patients who are at risk of developing foot ulceration is the cornerstone of disease management. Patients

should fully understand the risks posed by the loss of protective sensation or an inadequate blood supply to their feet. Education of the patient at risk may reduce the incidence of foot ulcers and subsequently amputations.

The patient at risk for foot ulceration should:

- Inspect his or her feet every day, including areas between toes. Inspection of the sole may be accomplished using a mirror.
- Let someone else inspect his or her feet in cases where the patient is unable to do it.
- Avoid walking barefoot any time, in- or outdoors.
- Avoid wearing shoes without socks, even for short periods.
- Buy shoes of the correct size.
- Avoid wearing new shoes for more than 1 h per day; feet should be inspected after taking off new shoes; in the case of foot irritation the patient should inform the healthcare provider.
- Change shoes at noon, and, if possible, again in the evening; this prevents high pressures remaining on the same area of the foot for a prolonged period.
- Inspect and palpate the inside of his or her shoes before wearing them.
- Wash his or her feet every day, taking care to dry them, especially the web spaces.
- Avoid putting his or her feet onto heaters.
- Test the water temperature before bathing using his or her elbow; the temperature of the water should be less than 37 °C.
- Avoid the use of chemical agents or plasters and razors for the removal of corns and calluses; they must be treated by a health care provider.
- Cut the nails straight across.
- Wear socks with seams inside out, or preferably without any seams at all.
- Use lubricating oils or creams for dry skin, but not between toes.
- Inspect his or her feet after prolonged walking.
- Notify his or her healthcare provider at once, if a blister, cut, scratch, sore, redness or black area develops, or if any discharge appears on socks.

RISK CATEGORY 2

Patients in this category do not usually need custom-made shoes. The use of appropriate *insoles*, which reduce peak plantar pressures under specific areas, is usually enough; these are inserted in commercially available extra-depth shoes. Insoles must be custom-molded and shock-absorbing. The idea is to redistribute plantar pressures by the use of such insoles, that is, to decrease the load from regions 'at-risk' to 'safe' regions. In addition, insoles reduce shear stress since total contact minimizes the horizontal and vertical foot movement. These insoles have two or three layers and are made of materials of different density. A thin layer of the material with the lowest density (the most potent shock-absorbing material, usually cross-linked polyethylene foams) is placed at the foot–insole interface; the firmest material (acrylic plastics, thermoplastic polymers or cork) is placed at the shoe–insole interface. A soft, shock-absorbing, durable material (closed cell neoprene, rubber or urethane polymer) is placed between them (Figures 2.11 and 2.12). Appropriate insoles for the patient at risk for ulceration should have a minimum thickness of 6.25 mm. Patients at high risk require thicker (12.5 mm) insoles.

RISK CATEGORY 3

These patients need the greatest help to remain free of foot ulceration. Patients in this

Figure 2.11 Upper side of a three-layer custom-made insole used to offload pressure on the forefoot. The upper layer is composed of cross-linked polyethylene foam, the middle layer of polyurethane, and the lower layer of cork

category are 12–36 times more likely to develop foot ulcers than patients in category 0. Severe foot deformities and limited mobility of the foot joints are associated with high plantar pressures.

Limited joint mobility is defined as a limitation in dorsiflexion of the first metatarsophalangeal joint of more than 50° when the patient is seated (hallux rigidus).

Patients with severe peripheral vascular disease are also included in this category. Inadequate circulation makes the thin skin vulnerable to ulceration.

In addition to custom-molded insoles, custom-made and extra depth-shoes are often necessary. Patients with recurrent foot ulcerations, or an active lifestyle, often need modifications of the outsole. In the *rocker* style shoe the rigid outsole rotates over a ridge (fulcrum) as the patient walks; this ridge is located 1 cm behind the metatarsal heads (see Figure 5.2). The rocker outsole allows the shoe to 'rock' forward during propulsion before the metatarsophalangeal joints are allowed to flex, thereby reducing the pressure applied to the forefoot. In a *roller* style shoe the contour of the outsole is a continuous curve without the ridge used in the rocker style. During walking, as the person lifts the heel, the shoe rolls forward on the curved outsole. This prevents the pressure from remaining in one region. Rocker style shoes are more effective in reducing forefoot plantar pressure than the roller style shoes.

METHODS FOR OFFLOADING PRESSURE ON THE FOOT

The mainstay in the management of an active plantar foot ulcer is the effective offloading of the ulcer area. Once an ulcer is

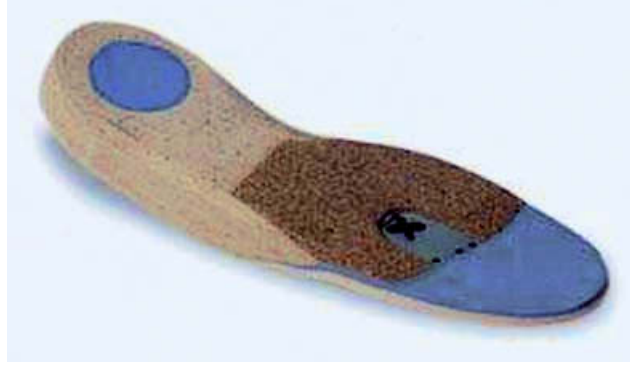

Figure 2.12 Lower side of insole illustrated in Figure 2.11

present, it will not heal unless the mechanical load on it is removed. Among the methods used for this purpose are complete bed rest, crutch-assisted gait, wheelchair, and prosthetics. However, these methods are impractical for the majority of patients to use for a period of several weeks while the ulcer heals. Common approaches for reducing the load on the ulcerated area include the use of a total-contact cast or other commercially-available casts, and therapeutic footwear.

TOTAL-CONTACT CAST

A total-contact cast (Figure 2.13) is a plaster of Paris cast, which extends from knee to toes. This is the method of choice for the treatment of grades 1 and 2 (according to the Meggitt–Wagner classification) diabetic foot ulcers which are located on the forefoot and midfoot; the cast reduces peak plantar pressures in these areas by almost 40–80%, but is less effective with ulcers located on the hindfoot. In one study, the use of a total-contact cast resulted in almost 90% of plantar ulcers healing within an average of 6–7 weeks. This method permits walking while uniformly decreasing the pressure on the sole of the foot.

Figure 2.13 Total-contact cast

The ulcerated area should be debrided and covered with a thin dry dressing. A total-contact cast is applied with the patient in the prone position and the foot and ankle in a neutral position (i.e. with the foot flexed at a 90°-angle to the ankle). A layer of fiberglass tape is usually applied over the plaster, to strengthen the cast and allow early ambulation. A small rubber rocker is added for walking. A plywood board is inserted between the rubber rocker and the cast in order to minimize the possibility of the sole of the cast becoming cracked. The cast should be changed every 3–7 days. The use of a total-contact cast is contraindicated when infection or gangrene (Meggitt–Wagner stages 3–5) is present. Skin atrophy and an ankle brachial index below 0.4 are considered to be relative contraindications to the use of a total-contact cast. Although a total-contact cast permits walking, patients are instructed to minimize their activity in order to reduce the pressure on their soles. Instability and the risk of falls are disadvantages of this cast. Both in- and outdoor compliance is another advantage, especially for the non-compliant patient, since this cast is not easily removed.

OTHER COMMERCIALLY-AVAILABLE CASTS

Removable Cast Walkers

Prefabricated walkers function on a similar principle to the total-contact cast and

are removable, commercially available, lightweight casts (see Figure 9.11). They are not designed to provide total contact, and the addition of inflatable or adjustable pads reduces movement of the limb within the cast. A custom-molded removable insole is adjusted to reduce plantar pressure. Use of removable cast walkers allows inspection and dressing of the wound on a daily basis. They may be used in patients with infected and ischemic ulcers. In addition, patients can bathe and sleep more comfortably. The rocker shape of the outsole reduces further pressure on the forefoot while standing and walking. In addition, these casts are ideal for clinics, which do not have personnel with experience in plastering.

Scotch-Cast Boot

This is a lightweight, well-padded fiberglass cast, extending from just below the toes to the ankle, and it is worn with a cast sandal (Figure 2.14). It may be fabricated as a removable or non-removable cast. With appropriate modifications of the pads, the scotch-cast boot reduces pressure on any region of the sole when needed. Removable scotch-cast boots can be used in cases of both ischemic and infected ulcers, since drainage and wound dressings are easily applied. As with the total-contact cast, experience in plastering is required.

PRESSURE RELIEF SHOES (THERAPEUTIC FOOTWEAR)

These are temporary shoes which allow some level of ambulation, while at the same time offloading pressure on the ulcerated area. These shoes are easy to use and are of low cost and since they enable the patient to walk quite normally, they lead

Figure 2.14 Scotch-cast boot

to a better quality of life. A rigid rocker sole is incorporated in order to reduce the weight-bearing load in the forefoot by up to 40% during walking. The appropriate choice of insole may reduce plantar pressure by an additional 20%. Half shoes (see Figure 3.36) are indicated for ulcers located on the forefoot (almost 90% of diabetic foot ulcers are located in this area). They offload pressure on the entire forefoot, while increasing pressure on the midfoot and heel, permitting the patient to engage in limited walking activities. Instability is a problem, and the patient needs to use crutches. With the use of half shoes the mean time to ulcer healing was reported to be 7–10 weeks in two studies. Patients are instructed to walk on their heel and avoid forefoot contact with the ground at the end of the stance phase. A sole lift

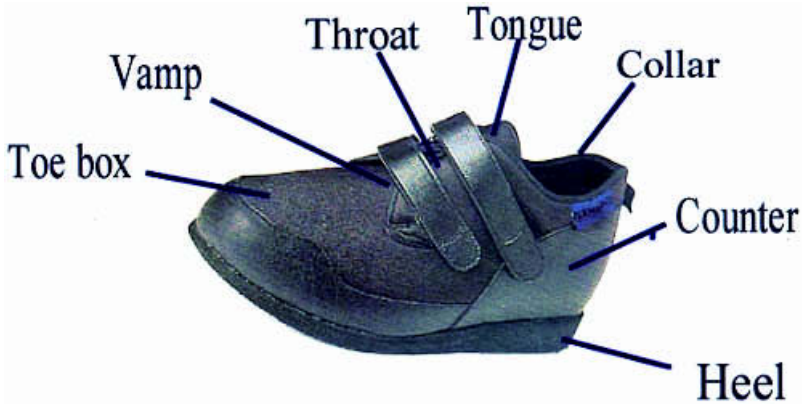

Figure 2.15 Shoe terms

on the opposite shoe may be necessary to equalize the limb length. These shoes are easily removed for dressing changes.

Heel-free shoes (see Figure 5.18) reduce peak plantar pressure on the heel by transferring pressures to the midfoot and forefoot. They have the same advantages and disadvantages as half shoes. Both half and heel-free shoes are commercially available.

Ulcers located on midfoot (mainly over bony prominences due to neuro-osteoarthropathy) are best treated with the use of customized insoles with windows under the ulcerated area.

Shoe terms are shown in Figure 2.15.

DRESSINGS

The characteristics required for optimal wound dressings have been described as follows. They should

- be free from particulate or toxic contaminants
- remove excess exudates and toxic components
- maintain a moist environment at the wound/dressing interface
- be impermeable to microorganisms, thus protecting against secondary infection
- allow gaseous exchange
- be easily removal without trauma
- be transparent, or changed frequently, thus allowing monitoring of the wound
- be acceptable to the patient, conformable and occupy a minimum of space in the shoe
- be cost-effective
- be available in hospitals and community health care centers

There is a broad spectrum of wound dressing materials currently available. Their particular properties and indications are described in Table 2.6 and the advantages and disadvantages of the available types of dressings are described in Table 2.7.

NEW TREATMENTS

HYPERBARIC OXYGEN

There have been no controlled trials comparing the use of hyperbaric oxygen therapy

Table 2.6 Properties, and indications of available dressings

Type of dressing	Necrosis/ slough	Gangre-nous	Infection	Low exudate	High exudate	Flat wound with low exudate	Flat wound with high exudates	Cavity without sinus	Cavity with sinus tract
Dry		+	+	+		+			
Enzymatic debrider	+								
Films				+		+			
Foams			+	+	+		+		
Hydrogels	+							+	+
Hydrocolloids				+		+		+	
Alginates			+		+	Alginate rope		Alginate rope	Alginate rope

Table 2.7 Advantages and disadvantages of available types of dressings

Type of dressing	Advantages	Disadvantages
Traditional dressings (gauze and absorbent cellulose)	Cheap and widely available. Appropriate for gangrenous lesions	Adhere to the wound bed and may cause bleeding on removal. Provide little protection against bacterial contamination
Films	Semi-permeable. Form bacterial barrier. Durable. Require changing every 4–5 days. Cheap	Useful on flat or superficial wounds only. Some patients are allergic to the adhesive in the dressing
Foams	Appropriate for ulcers with high production of exudates. Provide thermal insulation. Easily conformable. May be used to fill cavities without sinus tracts	Variability in absorbency of different foams. Limited published data
Hydrogels	Effective, versatile and easy to apply. Very selective, with no damage to surrounding skin. Safe process, using the body's own defense mechanisms. Promote autolysis and healing. Decrease risk of infection. Useful in removing slough from wounds. May be used to fill cavities with sinus tracts	Effect difficult to quantify. Not as effective and rapid as surgical debridement. Not appropriate for neuro-ischemic ulcers, which produce minimal exudates. Wound must be monitored closely for signs of infection
Hydrocolloids	Safe and selective, using the body's own defense mechanisms. Good for necrotic lesions, with light to moderate exudates. May be used to fill cavities without sinus tracts. Can be easily used with a shoe. Adhesive surface prevents slippage. Do not require daily dressing changes. Cost-effective	Their occlusive and opaque nature prevents daily observation of the wound. Wound must be monitored closely for signs of infection. May promote anaerobic growth and mask a secondary infection

(*continued overleaf*)

Table 2.7 (*continued*)

Type of dressing	Advantages	Disadvantages
Alginates	Useful as absorbents of exudates. Good for infected ulcers. Some products have hemostatic properties	Not appropriate for neuro-ischemic ulcers, which produce minimal exudates. Some researchers think they may traumatize the wound bed and predispose to infections. May dry out and form a plug within the wound bed. Requires painstaking removal with the use of large amounts of saline
Enzymatic debriders	Good for any wound with a large amount of necrotic debris, and for eschar formation. Promote autolysis and fast healing. Decrease maceration of the skin, and risk of infection	Costly. Must be applied carefully only to the necrotic tissue. May require a specific secondary dressing. Irritation and discomfort may occur
Medicated dressings		Data based on animal models and cell cultures only

in the treatment of neuropathic ulcers. At the present time it is only used to treat patients with severe foot infections which have not responded to other treatments. Hyperbaric oxygen is particularly effective in patients with foot ischemia.

FACTORS ACCELERATING WOUND HEALING

Platelet-Derived Growth Factor-β

Platelet-derived growth factor-β (PDGF-β, becaplermin, Regranex®, Janssen-Cilag) has been developed as a topical, effective and safe therapy for the treatment of diabetic foot ulcers and has also been found to be effective and safe as local therapy for the treatment of non-infected diabetic foot ulcers. It is applied as a gel on the ulcer surface once daily by the patient, while the ulcer is debrided on a weekly basis. A dose of 100 μg/g has been demonstrated to be the most effective. Compared to standard treatment, more ulcers treated with becaplermin heal completely and in a shorter time. The maximum time required to achieve has been reported as 20 weeks.

Dermagraf®

Dermagraf® (Smith & Nephew) is a bio-engineered 'human dermis' designed to replace the patient's own damaged dermis. It is applied to the ulcerated area on a weekly basis. Preliminary results show that it is an effective and safe treatment. According to a controlled trial, 50% of diabetic foot ulcers healed within 8 weeks when treated with Dermagraf, compared to 8% of ulcers treated with standard methods. Dermagraf should be stored at $-70\,^{\circ}$C and must be thawed, rinsed and cut to the size of the ulcer prior to implantation. As with becaplermin, the presence of infection is a contraindication to its use.

Graftskin

Graftskin (Apligraf®, Novartis) consists of an epidermal layer formed by human keratinocytes and a dermal layer, composed

of human fibroblasts derived from neonatal foreskin in a bovine collagen matrix. Studies have shown that treatment with Apligraf resulted in a higher percentage of diabetic foot ulcers healing completely and in a shorter time (56% of the ulcers healed in 65 days), compared to placebo (39% of the ulcers healed in 90 days). Apligraf has been shown to be safe and, in addition, its use was found to lead to a reduction in the incidence of osteomyelitis and amputations.

Granulocyte-Colony Stimulating Factor (GCSF)

Subcutaneous administration of GCSF once daily for 1 week in patients with infected foot ulcers resulted in a faster resolution of the infection, earlier eradication of bacterial pathogens isolated from wound swabs, shorter duration of i.v. antibiotic administration and shorter duration of hospital stay in a double-blind placebo-controlled study. Larger controlled studies are needed to evaluate the efficacy and safety of GCSF in the treatment of the infected foot ulcers.

Hyaff®

Hyaff® (Convatec, Bristol–Myers–Squibb) is a semi-synthetic ester of hyaluronic acid. Serum or wound exudates, when in contact with Hyaff, form a moist environment which promotes granulation and healing. So far it has been used in the treatment of neuropathic ulcers with promising results.

Keywords: Classification of foot ulcers; Meggitt–Wagner classification of foot ulcers; 'The University of Texas classification system for diabetic foot wounds'; neuro-ischemic ulcers, characteristics; ischemic ulcers, characteristics; neuropathic ulcers, characteristics; prevention of foot ulcers; risk category for foot ulcers; education in foot care; insoles; limited joint mobility; methods for offloading pressure on the foot; total-contact cast; manufactured casts; removable cast walkers; scotchcast boot; therapeutic footwear; heel-free shoes; half shoes; shoe terms; hyperbaric oxygen; platelet-derived growth factor-β; Dermagraf®; Graftskin; Apligraf®; granulocyte-colony stimulating factor; Hyaff®; dressings; dressings, advantages and disadvantages

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